REMARKS

The Office Action mailed July 29, 2005, has been received and reviewed. Claims 1-23 are currently pending in the application. Claims 9, 10, 12, 14 and 17-21 have been previously withdrawn from consideration. Claim 2 is objected to. Claims 1-8, 11, 13, 15, 16, 22 and 23 stand rejected. Applicants have amended claims 1, 16 and 22. Claims 2 and 23 have been cancelled. Applicants respectfully request reconsideration of the application as amended.

Priority

Applicants have requested a certified copy of the EP 01202569.8 application. It has not yet been received. Applicants will submit EP 01202569.8 once the certified copy is received.

Claim Objections

Claim 2 is objected to as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 2 has been cancelled thus mooting the objection.

Double Patenting

Claims 1-8, 11, 13, 15 and 22 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as assertedly being unpatentable over claims 1-5, 7, 12, 14 and 16 of co-pending application no. 10/303,157, in view of U.S. Patent 5,885,779 and further in view of Nicholson *et al.*

Applicants assert that the double patenting rejection is improper because claims 1-8, 11, 13, 15 and 22 of the claimed invention are not obvious and unpatentable over claims 1-5, 7, 12, 14 and 16 of co-pending application no. 10/303,157, in view of U.S. Patent 5,885,779 and further in view of Nicholson *et al.*

M.P.E.P. 706.02(j) sets forth the standard for an obviousness rejection, which standard is relied upon in this provisional obviousness-type double patenting rejection.

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the

> art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, **the prior art reference (or references when combined) must teach or suggest all the claim elements.** The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). (Emphasis added).

Claim 1 recites in part a recombinant receptor comprising an extracellular ligand-binding domain of a receptor; and a cytoplasmic domain, comprising a domain derived from a cytoplasmic domain of a receptor, **at least one activation site** and a heterologous bait polypeptide heterologous to the domain derived from a cytoplasmic domain of a receptor; wherein the activation of said recombinant receptor **is inhibited** by binding of a fusion protein to said heterologous bait polypeptide, said fusion protein comprising a prey polypeptide and at least one of an inhibitor of the activation of said recombinant receptor and a recruitment site for the inhibitor of the activation of said recombinant receptor. Applicants respectfully submit that application no. 10/303,157, U.S. Patent 5,885,779 ("the '779 patent") and Nicholson *et al.* do not teach or suggest all the elements of claims 1-8, 11, 13, 15 and 22.

More particularly, USSN 10/303,157 teaches an inactivated recombinant receptor, wherein a cytoplasmic domain activation site has been inactivated and that may be activated only by the binding of a ligand by the extracellular binding domain and the binding of a prey polypeptide to a heterologous bait peptide. The claims of USSN 10/303,157 do not teach or suggest all the elements of current claim 1 such as a functional activation site in the cytoplasmic domain and the inhibition of the active receptor by the binding of a prey polypeptide.

The Office alleges that "a receptor that is inhibited by prey binding would work just as well with these modifications as a receptor that is activated by prey binding." However, that is not the case. In USSN 10/303,157 the receptor is in a default inactivated condition and the substitution of the activation site on the fusion protein of USSN 10/303,157 with an inhibitor would not "work just as well" as the claimed invention.

The '779 Patent teaches a bait-fusion protein having a DNA-binding domain with a prey-fusion protein having a repression domain causing repression of specific reporter genes. (U.S.

Patent 5,885,779, column 5, lines 15-21). The '779 Patent does not teach a recombinant receptor comprising an extracellular ligand-binding domain and a cytoplasmic domain, the cytoplasmic domain comprising a heterologous bait polypeptide heterologous to the cytoplasmic domain.

Nicholson teaches that a Y to F point mutation on residue 757 of a chimeric gp130 receptor plays a role in gp130 inhibition by SOCS-3. However, Nicholson fails to teach or suggest a recombinant receptor comprising an extracellular ligand-binding domain of a receptor; and a cytoplasmic domain comprising a domain derived from a cytoplasmic domain of a receptor, wherein the cytoplasmic domain **comprises at least one activation site** and a heterologous bait polypeptide heterologous to the cytoplasmic domain of a receptor; wherein the activation of said recombinant receptor **is inhibited** by binding of a fusion protein to said heterologous bait polypeptide.

Therefore, no *prima facie* case of obviousness exists because USSN 10/303,157, the '779 patent and Nicholson *et al.* fail, alone or in combination, to teach or suggest all of the elements of the rejected claims.

Additionally, the policy behind judicially created obviousness-type double patenting is to prevent an effective timewise extension of the patent monopoly and avoid precluding the public from practicing the invention for longer than appropriate. In this case, applicants assert that the current double patenting rejection is an attempt to avoid a *non-existent* problem of patent term extension.

More particularly, the scope of claims 1-8, 11, 13, 15 and 22 may be practiced without infringing on the scope of the referenced claims from USSN 10/303,157. Independent claim 1 of the instant claims recites, in part, a recombinant receptor comprising an extracellular ligand-binding domain of a receptor; and a cytoplasmic domain, comprising a domain derived from a cytoplasmic domain of a receptor, wherein the cytoplasmic domain comprises at least one activation site and a heterologous bait polypeptide heterologous to the cytoplasmic domain of a receptor; wherein the activation of said recombinant receptor **is inhibited by binding** of a fusion protein to said heterologous bait polypeptide.

In contrast, independent claim 1 of the referenced USSN 10/303,157 recites in part that a recombinant receptor **is activated by binding** of a fusion protein to a heterologous bait

polypeptide. Accordingly, the claimed invention may be practiced without infringing on the claims of USSN 10/303,157.

Furthermore, the instant application is a continuation of PCT/EP02/07419, filed on July 2, 2002. The referenced USSN 10/303,157 is a continuation of PCT/EP01/05916, filed May 22, 2001. Accordingly, a patent resulting from the instant claims would expire after the potential patent from USSN 10/303,157. Accordingly, there is little possibility for a timewise extension of the patent monopoly in the claims beyond that of the referenced USSN 10/303,157.

Therefore, applicants request removal of the provisional double patenting rejection and ask reconsideration of the claims.

Claim Rejections—35 U.S.C. § 112, 1st paragraph, new matter

Claim 16 and 23 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that was allegedly not described in the specification in such way as to reasonably convey to one of skill in the art that the inventors had possession of the claimed invention. Claim 23 has been cancelled herein making this rejection moot for that claim.

Applicants respectfully submit that amended claim 16 correctly recites in part "bait polypeptide." Support for this bait polypeptide is found in paragraph [0025], page 9, of the specification.

Therefore the specification reasonably conveys to one of skill in the art that the inventors had the claimed invention at the time of filing. As such, applicants request removal of the rejection of claim 16 and reconsideration of the claims.

Claim Rejections—35 U.S.C. § 112, 2nd paragraph

Claims 1-8, 11, 13, 15, 16 and 23 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the claimed invention. Claim 23 has been cancelled herein making this rejection moot for that claim.

In regards to independent claim 1, applicants do not agree with the rejection but have amended claim 1 to remove any alleged ground for rejection.

More particularly, amended claim 1 recites in part a cytoplasmic domain, comprising a domain derived from a cytoplasmic domain of a receptor, at least one activation site and a heterologous bait polypeptide heterologous to the domain derived from a cytoplasmic domain of a receptor. The amendment makes it clear that the cytoplasmic binding domain is derived from a receptor and also comprises a heterologous bait polypeptide. Therefore, any alleged indefiniteness of claim 1, and those claims dependent therefrom, has been removed.

In regards to claim 16, applicants respectfully submit that amended claim 16 correctly recites in part "a bait polypeptide" and "a cytoplasmic domain," thus removing any alleged indefiniteness and insufficient antecedent basis.

As such, applicants submit that any alleged indefiniteness or insufficient antecedent basis has been removed and request withdrawal of the rejection and reconsideration of the claims.

Claim rejections—35 U.S.C. § 102(b)

Claims 1-5, 11, 13, 15, 16, 22 and 23 are rejected 35 U.S.C. § 102(b) as allegedly being anticipated by Medici *et al.* Claim 23 has been cancelled herein making this rejection moot for that claim. Applicants traverse this rejection and respectfully submit that Medici fails to disclose each and every element of the rejected claims.

Medici teaches a chimeric receptor composed of yeast STE2 G-protein-coupled receptor (GPCR) and a protein X. A GPCR has seven-transmembrane domains yielding four incongruous cytoplasmic domains. (Medici *et al.*, Fig. 6). GPCRs are trans-activators, *i.e.*, the target activation site **is located away from the receptor itself**, on another protein such as the G-protein. *Id.* The cytoplasmic domains of GPCRs have no cis-activating sites, *i.e.*, the target activation site is on the receptor itself. Medici also teaches a second fusion protein composed of Gα subunit coupled with protein Y. When proteins X and Y bind, this then brings the bound Gα subunit in sufficient proximity with the GPCR to activate the receptor.

Amended claim 1 recites in part a cytoplasmic domain, comprising a domain derived from a cytoplasmic domain of a receptor, at least one activation site and a heterologous bait polypeptide heterologous to the domain derived from a cytoplasmic domain of a receptor. Medici fails to expressly or inherently disclose a cytoplasmic domain comprising at least one activation

site.

More particularly, the claimed invention recites in part that the cytoplasmic domain of the receptor protein itself has the activation site and the catalytic receptor protein is naturally cis-acting on the activation site. Furthermore, the claimed invention recites in part that a normal activation site on the cytoplasmic domain is inactivated and replaced by an activation site situated on another protein. In contrast, the GPCRs of Medici do not have any activation sites on the cytoplasmic domain—the activation site of the GPCRs is on the G-protein.

Independent claim 22 recites in part a cytoplasmic domain comprising an intracellular domain, a bait polypeptide and **an activation site**. Again, as previously stated, Medici fails to expressly or inherently disclose a cytoplasmic domain comprising an activation site.

Furthermore, contrary to what was presented by the Office, it is not inherent in the receptor as taught by Medici that if a prey polypeptide comprising an inhibitor were bound to the bait portion of the receptor, that it would inhibit receptor activation. As discussed previously, the GPCRs of Medici do not have any activation sites on the cytoplasmic domain and Medici fails to disclose any bait proteins on the cytoplasmic domain. Therefore, the effect of a prey polypeptide comprising an inhibitor bound to the receptor of Medici would not be inherent—it would likely have no effect.

Therefore, Medici fails to disclose expressly or inherently each and every element of independent claims 1 and 22 and those claims dependent therefrom. Accordingly, applicants respectfully request removal of this rejection and kindly request reconsideration of claims.

Claim rejections—35 U.S.C. § 103

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Medici *et al.* in view of Osborne *et al.* Applicants respectfully traverse the rejections as hereinafter set forth.

A *prima facie* case of obviousness cannot be established because Medici in view of Osborne, fail to teach or suggest every claim element because claims 6-8 depend from and, thus, include the elements of amended, base claim 1. Namely, Medici and Osborne, alone or in combination, fail to teach or suggest a recombinant receptor comprising an extracellular ligand-binding domain of a receptor; and a cytoplasmic domain comprising a domain derived

from a cytoplasmic domain of a receptor, **at least one activation site** and a heterologous bait polypeptide heterologous to the domain derived from a cytoplasmic domain of a receptor.

Moreover, a person of skill in the art would have no motivation to combine the references or any expectation of success from combining Medici and Osborne. Medici is investigating membrane bound receptors in yeast, while Osborne is using the normal nuclear based yeast-two-hybrid and studying protein expression at the cytoplasmic level. Osborne's protein expression requires overexpression of kinase in yeast which would prove toxic in mammalian cells as used in the instant invention. Additionally, there are no cytokine or tyrosine kinase type receptors in yeast.

Accordingly, claims 6-8 are not obviousness in view of Medici and Osborne. Reconsideration and withdrawal of the obviousness rejection is requested.

CONCLUSION

In view of the foregoing amendments and remarks, the applicants submit the claims define patentable subject matter and a notice of allowance is requested. Should questions remain after consideration of the foregoing, the Office is kindly requested to contact the applicants' attorney at the address or telephone number herein.

Respectfully submitted,

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